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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/751,657	12/31/2000	Rolfe C. Anderson	1087.5A (39US2)	2968

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EXAMINER

BEISNER, WILLIAM H

ART UNIT PAPER NUMBER

1744

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/751,657

Applicant(s)

ANDERSON ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 45-48 and 66-114 is/are pending in the application.
- 4a) Of the above claim(s) 74,99 and 111-114 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 45-48, 66-110 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Newly submitted claims 74, 99 and 111-114 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The newly claimed embodiment encompassed by claims 74, 99 and 111-114, which corresponds to Figure 29 of the instant application, is a patentably distinct species with respect to the species encompassed by the originally filed claims and corresponds to Figures 41 or 42 of the instant specification.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 74, 99 and 111-114 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 66-110 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Claims 66-110 are newly recited claim limitations that recite additional structural elements in combination with the hybridization device of originally filed claims 45-48. Claims 45-48 correspond to the disclosed embodiment of "low volume hybridization system" and can be found in the lengthy specification beginning at column 51, line 38 and continues through column 52, line 45. Figures 41 and 42 correspond to this specific disclosure of "A low-volume hybridization device". New claims 66-110 recite additional features such as heaters, coolers, extraction chambers, base units, processing chambers, etc. See especially claims 74 and 99. Review of the disclosure encompassed by the text bridging column 51, line 38 through column 52, line 45 does not disclose the combination of the device of original claims 45-48 with the additional structures recited in claims 66-110. While the instant disclosure may individually disclose these elements used in other embodiments and/or combinations, the originally filed disclosure fails to convey, with reasonable clarity to those skilled in the art that, as of the filing date sought, applicants were in possession of the invention as now encompassed by claims 66-110. See *Ex parte Ohshiro*, 14 USPQ2d 1750.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 45-48, 71, 78-96 and 102-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrevski et al.(US 5,882,903) in view of Southgate et al.(US 5,863,502).

The reference of Andrevski et al. discloses a low-volume hybridization chamber device (See Figures 2B and 4A) that includes a base (210, 230, 252); a reaction chamber (250) disposed in the base and bound by a flexible diaphragm (241/251). The device includes a pressure chamber (321A) that is separated from the reaction chamber by flexible diaphragm (241/251).

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While the reference of Andrevski et al. discloses that hybridization reactions can be performed within the reaction chamber (250) (See column 19, lines 4-29), the reference is silent as to the use of a probe array in the reaction chamber.

The reference of Southgate et al. discloses that the use of a plurality of hybridization probes on a membrane (probe array) within a chamber of a microchannel device is known in the art (See column 24, line 66, to column 25, line 13).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ a hybridization probe array membrane in the chamber of the reference of Andrevski et al. for the known and expected result of providing an alternative means recognized in the art to detect nucleic acids. The use of a probe array allows multiple types of nucleic acids to be detected in a single reaction chamber. Note when a probe array is positioned within the chamber as suggested above and the volume of the chamber is changed by the membrane movement disclosed in Figures 4A-4C, the device is considered to be structurally the same as that instantly claimed and therefore inherently capable of facilitating hybridization. Note, movement of the diaphragm as disclosed by the reference of Andrevski et al. causes the volume of the chamber to change and causes relative motion between fluid in the chamber and any probes supported in the chamber. Also note that a probe array positioned within chamber (250) as suggested above would result in a device wherein the probe array is "mounted" to the base (210,230,252) and disposed over a surface (252) inside the chamber and wherein the flexible diaphragm (241,251) is disposed over the surface of the array.

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With respect to the claimed chamber volumes of claims 46 and 47, the reference of Andreovski et al. discloses 5 micro liters and 20 micro liters as possible chamber volumes (See column 9, lines 58-63).

With respect to the claimed pneumatic system for moving the diaphragm of claim 48, see the pneumatic system disclosed in Figs. 4A-4C which discloses moving the membranes (See column 5, lines 30-55).

With respect to the heating and cooling elements of claims 66-70, the reference of Andreovski et al. discloses the use of thermoelectric system (500A)(See column 6, lines 30-60; and column 14, lines 36-51).

With respect to claims 71, 78-96 and 102-110, the reference of Southgate et al. discloses that it is known in the art to provide a hybridization device in communication with other processing chambers including extraction chambers and/or amplification chambers (See Example 2). The reference also discloses the use of a base unit in combination with the cassette device that includes the auxiliary equipment required for control of the processing steps performed within the cassette device housing the reaction/processing chambers (See Figure 10 and column 18, line 55 to column 23, line 27).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ the hybridization chamber of the modified primary reference with additional processing chambers including nucleic acid extraction and/or amplification chambers for the known and expected result of processing the sample using means known in the art for processing a liquid sample prior to detection using nucleic acid hybridization.

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While the reference of Southgate et al. discloses the use of separation beads and wash liquids, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum manner in which to extract the nucleic acid sample and means for manufacture while maintaining the required purification and detection efficiencies.

Note the above references are applicable as prior art under 35 USC 102(e) since the instant claims only have benefit of the filing date of parent application US 09/005,985 filed 12 January 1998 and/or provisional application US 60/043,490 filed 10 April 1997. The disclosures of the earlier applications do not provide support for the instant claim language.

8. Claims 72, 73, 75-77, 79, 97, 98, 100, 101 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrevski et al.(US 5,882,903) in view of Southgate et al.(US 5,863,502) taken further in view of Wainwright et al.(US 5,876,918).

The combination of the references of Andrevski et al. and Southgate et al. has been discussed above.

The above claims differ by reciting that the extraction chamber includes a porous and/or compressible plug material.

The reference of Wainwright et al. discloses that the use of a plug structure to extract nucleic acids from a liquid sample is known in the art.

In view of this teaching, it would have been obvious to one of ordinary skill in the art to position a plug structure in the extraction zone of the primary for the known and expected result of providing an alternative means recognized in the art for achieving the same result, separation

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of an analyte from a liquid sample. Note, the reference of Wainwright et al. discloses that the use of a plug provides advantages over beads because of an increased surface area to volume ratio.

While the reference discloses the use of specific polymer materials, it would have been obvious to one of ordinary skill in the art to employ other porous or fibrous plug structures known in the art for binding nucleic acids, such as glass wool, for the known and expected advantage associated with the use of a plug material over the use of beads.

9. Claims 78, 80-86, 102 and 104-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrevski et al.(US 5,882,903) in view of Southgate et al.(US 5,863,502) taken further in view of Schnipelsky et al.(US 5,229,297).

The combination of the references of Andrevski et al. and Southgate et al. has been discussed above.

The above claims differ by reciting that the extraction chamber includes a textured surface and/or beads for binding nucleic acids.

The reference of Schnipelsky et al. discloses that it is known in the art to separate or isolate nucleic acids from a liquid sample using immobilized beads on a surface or using a packed column of beads (See column 12, line 36 to column 13, line 17).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to immobilize the beads in the microchamber of the primary reference in a manner as suggested by the reference of Schnipelsky et al. for the known and expected result of providing an alternative

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means recognized in the art to achieve the same result, providing a nucleic acid extraction surface in a microchamber device.

With respect to the composition of the beads, it would have been obvious to one of ordinary skill in the art to determine the optimum bead material from those known in the art for use in isolation of nucleic acids, including glass or porous glass or cellulose.

Response to Arguments

10. Applicant's arguments filed 6/3/05 have been fully considered but they are not persuasive.

11. In response to the 35 USC 112, first paragraph, rejection of record, Applicants argue that the general assertions contained in the text on page 9, line 26 and page 117, line 16, would have reasonably conveyed to one of ordinary skill in the art that the subject matter of claims 66-110 was in the possession of the inventors at the time of filing the application. Applicants further argue that "Surely, a person of ordinary skill in the art would be able to combine the device elements described in one document. After all, in the obviousness rejections, the Examiner combined two or three separate and distinct references and asserted that the person of ordinary skill in the art would be able to combine these three separate references."

Applicants' comments are not persuasive because, the originally filed disclosure does not specifically disclose and/or claim any of the further recited claim elements of claims 66-110 in combination with the claimed low volume hybridization device. See applicants' comments on page 6, second paragraph, that states "these claim elements were not only disclosed but also

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claimed (however, not claimed in combination with the claimed low volume hybridization device)". Nothing in applicants' comments establishes that the originally filed disclosure would have conveyed, **with reasonable clarity**, to those skilled in the art that, as of the filing date sought, applicants were in the possession of the invention as encompassed by claims 66-100. The issue at hand is not whether one of ordinary skill in the art would have known how to combine the disclosed elements to achieve a device encompassed by claims 66-110, but whether one of ordinary skill in the art at the time of filing of the disclosure would have recognized that the device encompassed by claims 66-110 was considered applicants invention. The Examiner is of the position that a general statement that "the devices can integrate several or all of the operations involved in sample acquisition and storage, sample preparation and sample analysis, within a single, miniaturized, integrated unit" embedded in a 121 page specification does not convey with **reasonable clarity** that the combination of elements as encompassed by claims 66-110 was applicants' invention at the time of filing the application. If this were the case, Applicants would be permitted, after filing the original disclosure, to claim new combinations of disclosed elements that were not previously disclosed as being used together.

12. With respect to the rejection of claims 45-48, 71, 78-96 and 102-110 over the combination of the references of Andrevski et al. and Southgate et al. under 35 USC 103, Applicants argue that the combination of the references is improper for the following reasons:

- i) The reference of Andrevski et al. does not disclose any probe array (See page 17 of the response dated 6/3/05).

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ii) The combination of Andrevski et al. and Southgate et al. would result in the probe array being positioned between membranes (241) and (242) or would be mounted onto one of the membranes but would not result in a probe array being mounted on the base as claimed (See page 18 of the response dated 6/3/05).

iii) The combination of Andrevski et al. and Southgate et al. does not disclose a flexible diaphragm separating the pressure chamber from the reaction chamber and constructed to change the volume of the reaction chamber by changing the distance between the array surface and the diaphragm surface.

In response to argument i) above, the Examiner has relied upon the combination of the references of Andrevski et al. and Southgate et al. to suggest the use of a probe array within the reaction chamber.

In response to argument ii) above, the Examiner maintains that the combination of the references as suggested in the rejection of record would result in a device wherein the probe array would be positioned on or mounted on membrane (242) which is considered to be part of the base and would result with the flexible diaphragm (241) being disposed over the surface of the probe array.

In response to argument iii) above, the application of pressure and vacuum as disclosed by the reference of Andrevski et al. results in fluid being displaced over the surface of the probe array when the chamber is being filled and emptied. Furthermore, the device is structurally capable of changing the volume of the chamber without a flow of fluid into or out of the reaction chamber.

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13. Applicants' amendments to claims 74 and 99 are sufficient to overcome the obviousness-type double patenting rejections of record.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



William H. Beisner
Primary Examiner
Art Unit 1744

WHB